

WHAT IS CLAIMED IS:

1 1. A vascular prosthesis comprising:
2 an expansible structure which is implantable within a body lumen; and
3 means on or within the structure for releasing mizoribine into the body lumen
4 to inhibit smooth muscle cell proliferation.

1 2. A prosthesis as in claim 1, wherein mizoribine is released at a rate
2 between 5 µg/day to 200 µg/day.

1 3. A prosthesis as in claim 1, wherein mizoribine is released at a rate
2 between 10 µg/day to 60 µg/day.

1 4. A prosthesis as in claim 1, wherein mizoribine is released at an initial
2 phase wherein a rate of mizoribine release is between 0 µg/day to 50 µg/day and a subsequent
3 phase wherein a rate of mizoribine release is between 5 µg/day to 200 µg/day.

1 5. A prosthesis as in claim 1, wherein mizoribine is released at an initial
2 phase wherein a rate of mizoribine release is between 5 µg/day to 30 µg/day and a subsequent
3 phase wherein a rate of mizoribine release is between 10 µg/day to 100 µg/day.

1 6. A prosthesis as in claim 1, wherein mizoribine is released at an initial
2 phase wherein a rate of mizoribine release is between 40 µg/day to 300 µg/day and a
3 subsequent phase wherein a rate of mizoribine release is between 1 µg/day to 100 µg/day.

1 7. A prosthesis as in claim 1, wherein mizoribine is released at an initial
2 phase wherein a rate of mizoribine release is between 40 µg/day to 200 µg/day and a
3 subsequent phase wherein a rate of mizoribine release is between 10 µg/day to 40 µg/day.

1 8. A prosthesis as in claim 1, wherein mizoribine is released at a constant
2 rate between 5 µg/day to 200 µg/day.

1 9. A prosthesis as in claim 1, wherein a total amount of mizoribine
2 release is in a range from 100 µg to 10 mg.

1 10. A prosthesis as in claim 1, wherein a total amount of mizoribine
2 release is in a range from 300 µg to 2 mg.

- 1 11. A prosthesis as in claim 1, wherein a total amount of mizoribine
2 release is in a range from 500 µg to 1.5 mg.
- 1 12. A prosthesis as in claim 1, wherein a mammalian tissue concentration
2 of mizoribine at an initial phase is within a range from 0 µg/mg of tissue to 100 µg/mg of
3 tissue.
- 1 13. A prosthesis as in claim 1, wherein a mammalian tissue concentration
2 of mizoribine at an initial phase is within a range from 0 µg/mg of tissue to 10 µg/mg of
3 tissue.
- 1 14. A prosthesis as in claim 1, wherein a mammalian tissue concentration
2 of mizoribine at a subsequent phase is within a range from 1 picogram/mg of tissue to 100
3 µg/mg of tissue.
- 1 15. A prosthesis as in claim 1, wherein a mammalian tissue concentration
2 of mizoribine at a subsequent phase is within a range from 1 nanogram/mg of tissue to 10
3 µg/mg of tissue.
- 1 16. A prosthesis as in claim 1, wherein the expansible structure is a stent or
2 graft.
- 1 17. A prosthesis as in claim 1, wherein the means for releasing mizoribine
2 comprises a matrix formed over at least a portion of the structure.
- 1 18. A prosthesis as in claim 17, wherein the matrix is composed of a
2 material which undergoes degradation.
- 1 19. A prosthesis as in claim 17, wherein the matrix is composed of a
2 nondegradable material.
- 1 20. A prosthesis as in claim 19, wherein mizoribine is released by
2 diffusion through the nondegradable matrix.
- 1 21. A prosthesis as in claim 17, wherein the matrix comprises multiple
2 layers, wherein at least one layer contains mizoribine and another layer contains mizoribine,
3 at least one substance other than mizoribine, or no substance.

1 22. A prosthesis as in claim 21, wherein the at least one substance other
2 than mizoribine is an immunosuppressive substance selected from the group consisting of
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,
4 and methotrexate.

1 23. A prosthesis as in claim 21, wherein the at least one substance other
2 than mizoribine is an agent selected from the group consisting of anti-platelet agent, anti-
3 thrombotic agent, and IIb/IIIa agent.

1 24. A prosthesis as in claim 1, wherein the means for releasing mizoribine
2 comprises a rate limiting barrier formed over at least a portion of the structure.

1 25. A prosthesis as in claim 24, wherein mizoribine is released by
2 diffusion through the rate limiting barrier.

1 26. A prosthesis as in claim 1, wherein the means for releasing mizoribine
2 comprises a reservoir on or within the structure containing mizoribine and a cover over the
3 reservoir.

1 27. A prosthesis as in claim 1, wherein mizoribine is on or within the
2 expansible structure.

1 28. A prosthesis as in claim 1, wherein mizoribine is disposed within a
2 matrix or rate limiting membrane.

1 29. A vascular prosthesis comprising:
2 an expansible structure which is implantable within a body lumen; and
3 a rate limiting barrier on the structure for releasing mizoribine into the body
4 lumen to inhibit smooth muscle cell proliferation;
5 wherein the barrier comprises multiple layers, each layer comprising parylast
6 or paralene and having a thickness in a range from 50 nm to 10 microns.

1 30. A prosthesis as in claim 29, wherein mizoribine is released at a rate
2 between 5 µg/day to 200 µg/day.

1 31. A prosthesis as in claim 29, wherein mizoribine is released at a rate
2 between 10 µg/day to 60 µg/day.

1 32. A prosthesis as in claim 29, wherein at least one layer contains
2 mizoribine and another layer contains mizoribine, at least one substance other than
3 mizoribine, or no substance.

1 33. A vascular prosthesis comprising:
2 an expansible structure;
3 a source of mizoribine on or within the structure, wherein the mizoribine is
4 released from the source when the expansible structure is implanted in a blood vessel; and
5 a source of at least one other substance in addition to mizoribine on or within
6 the structure, wherein the at least one additional substance is released from the source when
7 the expansible structure is implanted in a blood vessel.

1 34. A prosthesis as in claim 33, wherein the at least one additional
2 substance is an immunosuppressive substance selected from the group consisting of
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,
4 and methotrexate.

1 35. A prosthesis as in claim 33, wherein the at least one additional
2 substance comprises at least one agent selected from the group consisting of anti-platelet
3 agent, anti-thrombotic agent, and IIb/IIIa agent.

1 36. A prosthesis as in claim 33, wherein each source comprises a matrix,
2 rate limiting membrane, or reservoir.

1 37. A method for inhibiting restenosis in a blood vessel following
2 recanalization of the blood vessel, said method comprising:
3 implanting a vascular prosthesis in the blood vessel; and
4 releasing mizoribine into the blood vessel so as to inhibit smooth muscle cell
5 proliferation.

1 38. A method as in claim 37, wherein mizoribine is released at a rate
2 between 5 µg/day to 200 µg/day.

1 39. A method as in claim 37, wherein mizoribine is released at a rate
2 between 10 µg/day to 60 µg/day.

1 40. A method as in claim 37, wherein mizoribine is released within a time
2 period of 1 day to 45 days in a vascular environment.

1 41. A method as in claim 37, wherein mizoribine is released within a time
2 period of 7 days to 21 days in a vascular environment.

1 42. A method as in claim 37, further comprising releasing at least one
2 other substance in addition to mizoribine simultaneously with mizoribine release.

1 43. A method as in claim 37, further comprising releasing at least one
2 other substance in addition to mizoribine sequentially with mizoribine release.

1 44. A method as in claim 42 or 43, wherein the at least one additional
2 substance is an immunosuppressive substance selected from the group consisting of
3 rapamycin, mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin,
4 and methotrexate.

1 45. A method as in claim 37, wherein the releasing comprises delaying
2 substantial release of mizoribine for at least one hour following implantation of the
3 prosthesis.

1 46. A method as in claim 45, wherein delaying release comprises slowing
2 release from a reservoir with a material that at least partially degrades in a vascular
3 environment over said one hour.

1 47. A method as in claim 45, wherein delaying release comprises slowing
2 release with a matrix that at least partially degrades in a vascular environment over said one
3 hour.

1 48. A method as in claim 45, wherein delaying release comprises slowing
2 release with a nondegradable matrix that allows diffusion of mizoribine through the
3 nondegradable matrix after said one hour.

1 49. A method as in claim 45, wherein delaying release comprises slowing
2 release with a rate limiting barrier that allows diffusion of mizoribine through the barrier after
3 said one hour.

1 50. A method as in any one of claims 47-49, wherein the prosthesis is
2 coated with the matrix or barrier by spraying, dipping, deposition, or painting.

1 51. A method as in claim 37, wherein the prosthesis incorporates
2 mizoribine by coating, spraying, dipping, deposition, chemical bonding, or painting
3 mizoribine on the prosthesis.

1 52. A method for inhibiting restenosis in a blood vessel following
2 recanalization of the blood vessel, said method comprising:
3 implanting a vascular prosthesis in the blood vessel; and
4 releasing mizoribine and at least one other substance in addition to mizoribine
5 from the prosthesis when implanted in the blood vessel.

1 53. A method as in claim 52, wherein the at least one additional substance
2 is an immunosuppressive substance selected from the group consisting of rapamycin,
3 mycophenolic acid, riboflavin, tiazofurin, methylprednisolone, FK 506, zafurin, and
4 methotrexate.

1 54. A method as in claim 53, wherein the immunosuppressive substance is
2 mycophenolic acid.

1 55. A method as in claim 53, wherein the immunosuppressive substance is
2 methylprednisolone.

1 56. A method as in claim 55, wherein mizoribine is released within a time
2 period of 1 day to 45 days and methylprednisolone is released within a time period of 2 days
3 to 3 months.

1 57. A method as in claim 52, wherein the at least one additional substance
2 comprises at least one agent selected from the group consisting of anti-platelet agent, anti-
3 thrombotic agent, and IIb/IIIa agent.

1 58. A method as in claim 52, wherein mizoribine and the at least one
2 additional substance are released simultaneously.

1 59. A method as in claim 52, wherein mizoribine and the at least one
2 additional substance are released sequentially.